AMENDMENTS TO THE SPECIFICATION

Prior to an examination of the above-identified patent application, the Examiner is respectfully requested to amend the Specification, as follows:

Please replace the paragraph appearing at page 1, line 16 (second paragraph starting in the Background Art section) to page 2, line 2, with the following amended paragraph:

It has been known that the degree of appearance of two characteristic pathological changes of Alzheimer disease well correlates to the degree of intellectual dysfunction. Therefore, researches have been conducted from early 1980's to reveal the cause of the disease through molecular level investigations of components of the two pathological changes. Senile plaques accumulate extracellularly, and β amyloid protein has been elucidated as their main component (abbreviated as "Aβ" hereinafter in the specification: Biochem. Biophys. Res. Commun., 120, ~~855~~ 885 (1984); EMBO J., 4, 2757 (1985); Proc. Natl. Acad. Sci. USA, 82, 4245 (1985)). In the other pathological change, i.e., the neurofibrillary tangles, a double-helical filamentous substance called paired helical filament (abbreviated as "PHF" hereinafter in the specification) accumulate intracellularly, and tau protein, which is a kind of microtubule-associated protein specific for brain, has been revealed as its main component (Proc. Natl. Acad. Sci. USA, 85, 4506 (1988); Neuron, 1, 827 (1988)).

Please replace the paragraph appearing at page 8, line 24 to page 9, line 8, with the following amended paragraph:

When the benzene ring, the naphthalene ring, the phenoxy group, the phenylamino group are substituents of the C_1-C_8 alkyl group represented by R^2, mentioned here above, they may have one or more substituents selected from the group consisting of a C_1-C_5 alkyl group such as methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, sec-butyl group, tert-butyl group, pentyl group, isopentyl group, neopentyl group, 1,1-dimethylpropyl group; a C_3-C_6 cycloalkyl group such as cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group; ~~hydroxy group;~~ a C_1-C_5 alkoxyl group such as methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, isobutoxy group, tert-butoxy group, pentyloxy group, and isopentyloxy group; a C_1-C_5 alkylthio group such as methylthio group, ethylthio group, propylthio group, butylthio group, and pentylthio group; a halogen atom such as fluorine atom, chlorine atom, bromine atom, and iodine atom; a C_1-C_5 halogenated alkyl group such as trifluoromethyl group; hydroxyl group; cyano group; amino group.

Please replace the paragraph appearing at page 28, lines 2-18, with the following amended paragraph:

The ~~2-thiopyrimidone~~ 2-mercaptopyrimidone represented by the above formula (XI) is prepared easily by a modification of the method described in EP 354,179. The reaction is carried out in the presence of a base such as sodium hydroxide, potassium hydroxide, sodium methoxide, sodium ethoxide, potassium t-butoxide, sodium carbonate, sodium hydrogencarbonate, potassium carbonate, triethylamine, diisopropylethylamine, and 1,8-diazabicyclo[5,4,0]undec-7-en for 1 to 100 hours at a suitable temperature ranging from 0°C to 200°C under nitrogen or argon atmosphere or under ordinary air to afford the desired compound (XI). Examples of a solvent for the reactions include, for example, alcoholic solvent such as methanol, ethanol, 1-propanol, isopropanol, tert-butanol, ethylene glycol, propylene glycol; etheric solvents such as diethyl ether, tert-butyl methyl ether, tetrahydrofuran, isopropyl ether; hydrocarbonic solvents such as benzene, toluene, xylene; halogenated hydrocarbonic solvents such as dichloromethane, chloroform, dichloroethane; aprotic polar solvents such as formamide, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, dimethyl sulfoxide, sulfolane, hexamethylphosphoric triamide, water and the like. Generally, a single solvent or a mixture of two or more solvents may be used so as to be suitable to a base used.

Please replace the paragraph appearing at page 28, line 29 to page 29, line 1, with the following amended paragraph:

Then the ~~2-thiopyrimidone~~ 2-mercaptopyrimidone derivative (XI) is transformed into the 2-chloropyrimidone (XII) by a chlorinating agent. The reaction time and temperature depend on the chlorinating agent used. Examples of a chlorinating agent for the reactions include, for example, thionyl chloride, thionyl chloride and dimethylformamide, phosphorus oxychloride, phosphorus oxychloride and dimethylformamide, oxalyl chloride, phosphorous oxychloride and dimethylformamide, and phosphorus pentachloride.

Please replace the paragraph appearing at page 34, lines 5-21, with the following amended paragraph:

A mixture of 2-chlorophenylboronic acid (5.0 g), 3-bromopyridine (4.8 g) and tetrakis(triphenylphosphine)palladium(0) (1.0 g) in toluene (47 ml), aqueous 2 M sodium carbonate solution (35 ml) and ethanol (2.4 ml) was heated under reflux for 5.5 h. The reaction mixture was cooled, and the toluene layer was separated. The aqueous layer was extracted with ethyl acetate and the combined organic extracts were dried ($MgSO_4$), filtered, and the filtrate evaporated under reduced pressure to give crude 3-(2-chlorophenyl)pyridine (7.9 g). To a solution of the 3-(2-chlorophenyl)pyridine (7.9 g) in dichloromethane (50 ml) was added iodomethane (3.8 ml) and the mixture was stirred for 15 h. The solvent was evaporated under reduced pressure and the obtained residue

was crystallized from ethyl acetate to give a pale-yellow crystal. To a solution of the obtained crystals in methanol (60 ml) was added sodium borohydride (1.7 g) under ice-cooling, and the mixture was stirred at room temperature for 3 h. The mixture was quenched with a saturated aqueous sodium chloride solution. The mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to give a crude 5-(2-chlorophenyl)-1,2,3,6-tetrahydro-1-methylpyridine (5.9 g).

Please replace the paragraph appearing at page 36, lines 4-20, with the following amended paragraph:

A mixture of 2-chlorophenylboronic acid (5.0 g), 3-bromopyridine (4.8 g) and tetrakis(triphenylphosphine)palladium(0) (1.0 g) in toluene (47 ml), aqueous 2 M sodium carbonate solution (35 ml) and ethanol (2.4 ml) was heated under reflux for 5.5 h. The reaction mixture was cooled, and the toluene layer was separated. The aqueous layer was extracted with ethyl acetate and the combined organic extracts were dried ($MgSO_4$), filtered, and the filtrate evaporated under reduced pressure to give crude 3-(2-chlorophenyl)pyridine (7.9 g). To a solution of the 3-(2-chlorophenyl)pyridine (7.9 g) in dichloromethane (50 ml) was added iodomethane (3.8 ml) and the mixture was stirred for 15 h. The solvent was evaporated under reduced pressure and the obtained residue was crystallized from ethyl acetate to give a pale-yellow crystal. To a solution of the obtained crystals in methanol (60 ml) was added sodium borohydride (1.7 g) under ice-

cooling, and the mixture was stirred at room temperature for 3 h. The mixture was quenched with a saturated aqueous sodium chloride solution. The mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to give a crude 5-(2-chlorophenyl)-1,2,3,6-tetrahydro-1-methylpyridine (5.9 g).

Please replace the paragraph appearing at page 36, line 21 to page 37, line 8, with the following amended paragraph:

To a solution of the 5-(2-chlorophenyl)-1,2,3,6-tetrahydro-1-methylpyridine (5.9 g) in dichloromethane (60 ml) was added 1-chloroethyl chloroformate (5.1 ml) and the mixture was stirred for 2.5 h. The mixture was washed with water and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate and the solvent was evaporated under reduced pressure to give brown oil. A solution of the obtained oil in methanol was refluxed for 2 h. The solvent was evaporated under reduced pressure and the obtained residue was crystallized from ethyl acetate to give 5-(2-chlorophenyl)-1,2,3,6-tetrahydropyridine hydrochloride (2.4 g). A solution of 5-(2-chlorophenyl)-1,2,3,6-tetrahydropyridine hydrochloride (155 mg), ~~2-chloro-1,6-dihydro-1-methyl-6-oxo-4-(pyridin-4-yl)pyrimidine~~ 2-chloro-1,6-dihydro-1-methyl-6-oxo-4-(pyrimidin-4-yl)pyrimidine (150 mg) and triethylamine (235 µl) in dimethylformamide (3 ml) was stirred at room temperature for 2 h. To the reaction mixture was added water

(3 ml), and the precipitated crystals were collected by filtration to give the title compound (240 mg) as white crystals.

^{1}H-NMR ($CDCl_3$) δ: 2.56(m, 2H), 3.52(m, 2H), 3.56(s, 3H), 4.09(m, 2H), 5.88(m, 1H), 7.21-7.29(m, 4H), 7.39(m, 1H), 8.13(d, *J* = 5.1 Hz, 1H), 8.82(d, *J* = 5.1 Hz, 1H), 9.25(s, 1H)

MS: 379(M+)

Please replace the paragraph appearing at page 37, lines13-20, with the following amended paragraph:

5-(2,6-dimethoxyphenyl)-1,2,3,6-tetrahydropyridine hydrochloride was prepared from 2,6-dimethoxyphenylboronic acid in the same manner as in Example 1. A solution of 5-(2,6-dimethoxyphenyl)-1,2,3,6-tetrahydropyridine hydrochloride (172 mg), ~~2-chloro-1,6-dihydro-1-methyl-6-oxo-4-(pyridin-4-yl)pyrimidine~~ 2-chloro-1,6-dihydro-1-methyl-6-oxo-4-(pyrimidin-4-yl)pyrimidine (150 mg) and triethylamine (235µl) in dimethylformamide (6 ml) was stirred at room temperature for 3 h. To the reaction mixture was added water (10 ml), and the precipitated crystals were collected by filtration to give the title compound (260 mg) as white crystals.